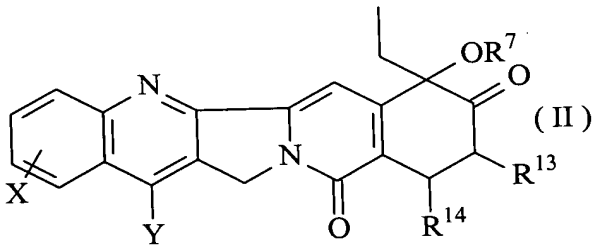
REMARKS/ARGUMENTS

Claims 1-4 and 6-20 are present in this application, claim 5 having been cancelled by the present amendment. Claims 12, 14 and 15 stand withdrawn. Claim 1 has been amended to delete various meanings for the definitions of X and Y, and to delete non-elected subject matter, in an effort to further prosecution of the present application. New claim 16 corresponds to original claim 1, wherein non-elected subject matter has been deleted, and the definitions of X and Y have been separately stated, with X having its original definition from original claim 1 (with the exception of the deletion of non-elected embodiments) and Y corresponding to the definition of Y in newly amended claim 1 (with non-elected embodiments and various other substituents definitions deleted). New claims 17-20 correspond to original claims 12-15, but depend on new claim 16 rather than original claim 1. The amendments are supported by the original claims. No new matter has been added by these amendments.

The present invention relates to a camptothecin analog having the structure:



where

X and Y are each independently SH, S-C_{1-6} alkyl, NH-C_{1-6} alkyl, -CHO, N_3,

-Z-$(CH_2)_a$-N-$((CH_2)_bOH)_2$, wherein Z is selected from the group consisting of O, NH and S, and a and b are each independently an integer of 2 or 3,

-Z-$(CH_2)_a$-N-$(C_{1-6}$ alkyl$)_2$ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3, or

$-CH_2-L$, where L is halogen (F, Cl, Br, I), $^+N_2$, $^+(OR^1)_2$, $^+S(R^1)_2$, $^+N(R^1)_3$, $OC(O)R^1$, OSO_2R^1, OSO_2CF_3, $OSO_2C_4F_9$, C_{1-6} alkyl-C(=O)-, C_{4-18} aryl-C(=O)-, C_{1-6} alkyl-SO_2-, perfluoro C_{1-6} alkyl-SO_2- or C_{4-18} aryl-SO_2-, (where each R^1 independently is C_{1-6} alkyl, C_{4-18} aryl or C_{4-18} ArC_{1-6} alkyl);

R^7 is H;

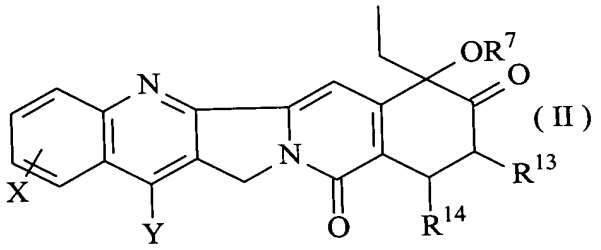
R^{13} and R^{14} are each H or combine to form a double bond;

and

n is an integer of 1 or 2,

and salts thereof.

New claim 16 claims the present invention as a camptothecin analog having the structure:



(II)

where

X is NO_2, NH_2, H, F, Cl, Br, I, COOH, OH, O-C_{1-6} alkyl, SH, S-C_{1-6} alkyl, CN, NH-C_{1-6} alkyl, N(C_{1-6} alkyl)$_2$, CHO, C_{1-8} alkyl, N_3,

$-Z-(CH_2)_a-N-((CH_2)_bOH)_2$, wherein Z is selected from the group consisting of O, NH and S, and a and b are each independently an integer of 2 or 3,

$-Z-(CH_2)_a-N-(C_{1-6}$ alkyl$)_2$ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3,

$-CH_2-L$, where L is halogen (F, Cl, Br, I), $^+N_2$, $^+(OR^1)_2$, $^+S(R^1)_2$, $^+N(R^1)_3$, $OC(O)R^1$, OSO_2R^1, OSO_2CF_3, $OSO_2C_4F_9$, C_{1-6} alkyl-C(=O)-, C_{4-18} aryl-C(=O)-, C_{1-6} alkyl-SO_2-, perfluoro C_{1-6} alkyl-SO_2- or C_{4-18} aryl-SO_2-, (where each R^1 independently is C_{1-6} alkyl, C_{4-18} aryl or C_{4-18} ArC_{1-6} alkyl); or

$-CH_2NR^2R^3$, where (a) R^2 and R^3 are, independently, hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-6} alkyl, C_{2-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkoxy C_{1-6} COR^4

where R^4 is hydrogen, C_{1-6} alkyl, perhalo C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-6} alkyl, C_{2-6} alkenyl, hydroxyl-C_{1-6} alkyl, C_{1-6}-alkoxy, or C_{1-6} alkoxy-C_{1-6} alkyl;

Y is SH, S-C_{1-6} alkyl, NH-C_{1-6} alkyl, -CHO, N_3,

-Z-$(CH_2)_a$-N-$((CH_2)_bOH)_2$, wherein Z is selected from the group consisting of O, NH and S, and a and b are each independently an integer of 2 or 3,

-Z-$(CH_2)_a$-N-(C_{1-6} alkyl)$_2$ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3, or

-CH_2-L, where L is halogen (F, Cl, Br, I), $^+N_2$, $^+(OR^1)_2$, $^+S(R^1)_2$, $^+N(R^1)_3$, $OC(O)R^1$, OSO_2R^1, OSO_2CF_3, $OSO_2C_4F_9$, C_{1-6} alkyl-C(=O)-, C_{4-18} aryl-C(=O)-, C_{1-6} alkyl-SO_2-, perfluoro C_{1-6} alkyl-SO_2- or C_{4-18} aryl-SO_2-, (where each R^1 independently is C_{1-6} alkyl, C_{4-18} aryl or C_{4-18} ArC_{1-6} alkyl);

R^7 is H;

R^{13} and R^{14} are each H or combine to form a double bond;

and

n is an integer of 1 or 2,

and salts thereof.

These compounds are useful in the treatment of various forms of cancer, primarily due to their activity as an inhibitor of Topoisomerase I.

The Examiner has restricted the claims of the present invention, classifying the claims into the following groups:

Group I: Claims 1-11, 13 in part, drawn to compounds and pharmaceuticals wherein R7 is a CO...substituents and R10 or R11 is an amino acid.

Group II: Claims 1-11, 13 in part, drawn to compounds and pharmaceutical compositions of formula I, where W, X, Y, R13 and R14 do not contain a hetero ring and R7 is a hydrogen.

Group III: Claims 1-11, 13 in part, drawn to compounds and pharmaceutical compositions of formula II wherein R7 is a hydrogen and all other X, Y, R13 and R14 substituents do not contain a hetero ring.

Group IV: Claims 1-11, 13 in part, drawn to compounds and pharmaceutical compositions not covered by any of the groups I-III as given above.

Group V: Claims 12, 14 drawn to methods of treating using these compounds

Group VI: Claim 15, drawn to a process of making the compounds.

Applicants hereby affirm the election, with traverse, of Group III, claims 1-11, 13 for compounds and pharmaceutical compositions wherein R7 is hydrogen and all other X, Y, R13 and R14 substituents do not contain a hetero ring.

Applicants note that in order for restriction to be proper, the Office must support any asserted restriction by showing that the claims of the restricted groups are patentably distinct and that search of all claims would present an undue burden. Applicants respectfully traverse the restriction on the grounds that the Office has not provided sufficient reasons to support the conclusion of patentable distinctness between the restricted groups.

The Examiner has classified Groups I-IV as being unrelated, on the basis that they are not disclosed as being capable of use together and have different modes of operation, different functions or different effects. In support of this assertion, the Examiner has stated that the inventions have different cores (formula I vs. formula II) and the various substituents have different properties and different bonding. However, Applicants note that both formula I and formula II are camptothecin derivatives, thus sharing the camptothecin core. While it is true that the substituents have different bonding and possibly different properties, there is nothing of record to indicate that this is sufficient to rise to the level of patentable distinctness, particularly when the compounds of the claims are all useful for performing the same function of inhibition of topoisomerase I, and in the treatment of various cancers. Accordingly, the Examiner has not provided sufficient reasons to support the conclusion of patentable distinctness and the restriction is therefore improper.

The Examiner has classified Groups I-IV and V as being related as product and process of use. The Examiner concludes that these are patentably distinct on the basis that there are other drugs that can be used to treat leukemia or tumors. However, the standard for patentable distinctness requires that the Examiner show that the process as claimed can be practiced with another materially different product. However, the process as claimed specifically requires the use of the present invention product. Further, the Examiner has provided no indication of what other drugs can be used in the claimed process, nor any indication of how those drugs are materially different from the present invention compounds. Accordingly, the restriction is improper and should be withdrawn.

Applicants note that the Examiner has not provided any reasons for requiring restriction between any of Groups I-V and Group VI. As such, this restriction should also be withdrawn.

Applicants note that upon allowance of claims to the present invention products, the invention of Groups V and VI should be rejoined, as each of the claims of these groups specifically depends from independent claim 1, and thus includes all limitations from that claim.

The elected claims 1-11 and 13 stand rejected under 35 U.S.C. 102(b) over EP 1101765 to Lavielle et al. (Applicants note that US 6,509,345 corresponds to and claims priority from the same French patent application FR 99-14499 to which the EP application claims priority). For the Examiner's convenience, Applicants also provide herewith a copy of a translation of the New Zealand application corresponding to the Lavielle EP application. Applicants note that Lavielle discloses various camptothecin compounds bearing a wide range of substituents. However, in the position corresponding to the present invention substituent Y, Lavielle nowhere discloses or suggests the substituents as now claimed, namely Lavielle nowhere discloses or suggests that their substituent at position R1 of Lavielle (corresponding to substituents Y of the present invention compounds) can be

SH, S-C_{1-6} alkyl, NH-C_{1-6} alkyl, -CHO, N_3,

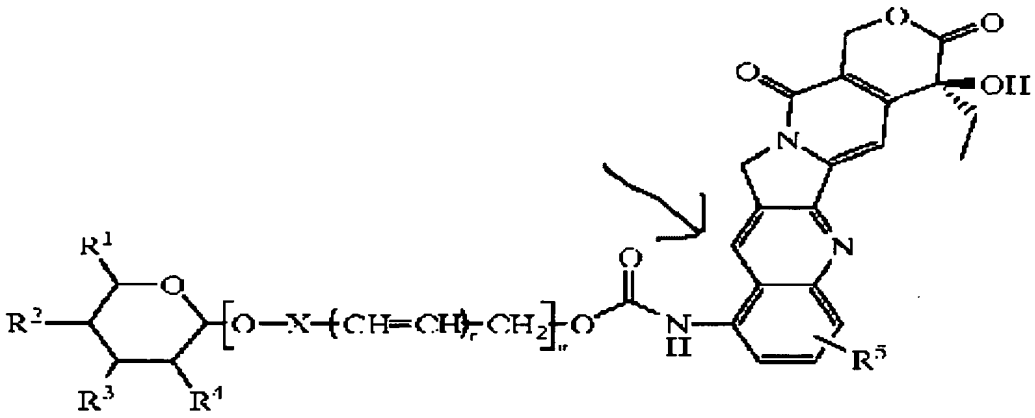
-Z-$(CH_2)_a$-N-$((CH_2)_bOH)_2$, wherein Z is selected from the group consisting of O, NH and S, and a and b are each independently an integer of 2 or 3,

-Z-$(CH_2)_a$-N-$(C_{1-6}$ alkyl$)_2$ wherein Z is selected from the group consisting of O, NH and S, and a is an integer of 2 or 3, or

-CH_2-L, where L is halogen (F, Cl, Br, I), $^+N_2$, $^+(OR^1)_2$, $^+S(R^1)_2$, $^+N(R^1)_3$, $OC(O)R^1$, OSO_2R^1, OSO_2CF_3, $OSO_2C_4F_9$, C_{1-6} alkyl-C(=O)-, C_{4-18} aryl-C(=O)-, C_{1-6} alkyl-SO_2-, perfluoro C_{1-6} alkyl-SO_2- or C_{4-18} aryl-SO_2-, (where each R^1 independently is C_{1-6} alkyl, C_{4-18} aryl or C_{4-18} ArC_{1-6} alkyl).

As such, Lavielle cannot anticipate the claims as now amended. Further, since there is no teaching or suggestion to modify the compounds of Lavielle to achieve the substituents as noted above for their position R1 (the present invention substituent Y), Lavielle cannot render the present invention as claimed obvious. Accordingly, this rejection should be withdrawn.

The claims also stand rejected under 35 U.S.C. 102(b) over Roffler et al. Roffler et al disclose various proactive antitumor compounds having the following formula:



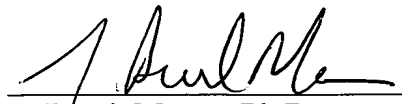
Applicants note that in this formula the position corresponding to substituent Y in the present invention (marked by the arrow in the above figure) can only be hydrogen. Throughout the entire Roffler et al reference this is the only possibility for that position of the compound. As such, since the claims as now amended exclude the possibility that Y can be hydrogen in the present invention, Roffler et al cannot anticipate the present invention. Accordingly the rejection should be withdrawn.

The claims stand further rejected under 35 U.S.C. 103 over EP 1101765 (Lavielle), and its US counterparts, and Roffler et al. As noted above, the present invention as now claimed, limits the definition of substituent Y in Claim 16, and both the definitions of substituents X and Y in claim 1, such that Y cannot be hydrogen and Y cannot be any of the substituents specified for position R1 of Lavielle's compounds. Since neither reference contains any teaching or suggestion to modify their compounds such that the substituent at the position corresponding to Y in the present invention can be any of the required definitions of the claims as now amended, and one of ordinary skill in this art would not be motivated to alter the compounds of Lavielle or Roffler in such a way, this rejection should be withdrawn.

Applicants submit that the application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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